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High doses of dextromethorphan induced shock and convulsions in a 19-year-old female: A case report


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Abstract

BACKGROUND

Dextromethorphan is a prevalent antitussive agent that can be easily obtained as an over-the-counter medication. There has been a growing number of reported cases of toxicity in recent years. Generally, there are numerous instances of mild symptoms, with only a limited number of reports of severe cases necessitating intensive care. We presented the case of a female who ingested 111 tablets of dextromethorphan, leading to shock and convulsions and requiring intensive care that ultimately saved her life.

CASE SUMMARY

A 19-year-old female was admitted to our hospital via ambulance, having overdosed on 111 tablets of dextromethorphan (15 mg) obtained through an online importer in a suicide attempt. The patient had a history of drug abuse and multiple self-inflicted injuries. At the time of admission, she exhibited symptoms of shock and altered consciousness. However, upon arrival at the hospital, the patient experienced recurrent generalized clonic convulsions and status epilepticus, necessitating tracheal intubation. The convulsions were determined to have been caused by decreased cerebral perfusion pressure secondary to shock,
and noradrenaline was administered as a vasopressor. Gastric lavage and activated charcoal were also administered after intubation. Through systemic management in the intensive care unit, the patient’s condition stabilized, and the need for vasopressors ceased. The patient regained consciousness and was extubated. The patient was subsequently transferred to a psychiatric facility, as suicidal ideation persisted.

**CONCLUSION**

We report the first case of shock caused by an overdose of dextromethorphan.

**Key Words:** Dextromethorphan; Drug overdose; Shock; Symptom; Treatment; Case report

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**Core Tip:** Prior studies have posited that dextromethorphan acts as a voltage-gated calcium channel inhibitor, one of its mechanisms of action. It is possible that the high dose in the present case amplified this effect. Previous reports attributed fatalities to central nervous system and respiratory depression, yet shock may also be a contributing factor, as evidenced by this case. This may be a rare occurrence, as it was only observed in the emergency room. We reported the first case of shock caused by an overdose of dextromethorphan. We were able to save the patient’s life in intensive care.


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**INTRODUCTION**

Dextromethorphan is a readily obtainable and broadly used over-the-counter antitussive drug, and recent years have seen more and more poisoning cases related to dextromethorphan consumption[1-5]. Recreational dextromethorphan consumption in the United States is prevalent among younger generations. Each year, roughly a million individuals aged 12-25 years abuse it non-medicinally[6]. As a result, there are over 6000 emergency department visits in the United States each year caused by dextromethorphan abuse, and half of all dextromethorphan-toxicity-caused emergency department visits occurred in patients aged 12-20 years[7]. Other countries, including Canada, Germany, Thailand, South Korea, and Japan, have also documented similar increases in dextromethorphan abuse cases[8-12].

More broadly, there have been many instances involving mild symptoms; only a small fraction of these reports are for severe cases that necessitated intensive care[13]. We presented the case of a female who ingested 111 tablets of dextromethorphan of Chinese origin, leading to shock and convulsions. She was transported to the emergency room (ER) and requiring intensive care, which ultimately saved her life. We also reported the first case of shock caused by an overdose of dextromethorphan (Figure 1).

**CASE PRESENTATION**

**Chief complaints**

A 19-year-old Japanese female presented to the ER with a complaint of disturbance of consciousness.

**History of present illness**

The symptoms started 2 h before presentation.

**History of past illness**

The patient ingested 111 tablets of dextromethorphan (15 mg) of Chinese origin, obtained through an online importer, in a suicide attempt approximately 2 h prior to presentation. The patient’s boyfriend discovered that she was lethargic. Once he saw an empty medication bottle, the patient was promptly transported to our hospital via ambulance.
Personal and family history
The patient had a history of previous drug overdose and multiple self-inflicted injuries resulting from jumping.

Physical examination
Upon physical examination, vital signs were as follows: body temperature of 37.7 °C; blood pressure of 82/44 mmHg; heart rate of 120 beats per minute; respiratory rate of 16 breaths per minute; E4V2M4/GCS10; and oxygen saturation of 96% on room air. The radial artery was barely perceptible upon palpation; nonetheless, the extremities were warm.

Her skin was dry, and her pupils were 6 mm/6 mm and reactive. She was drowsy and had difficulty conversing. The muscle tone in her limbs was normal, with no stiffness.

Laboratory examinations
Serum creatine phosphokinase was 106 U/L, and white blood count was 10100/mm³. The remainder of the complete blood count, prothrombin time, liver function tests, electrolytes, blood urea nitrogen and creatinine were all within normal limits.

Findings from venous blood gas analysis indicated lactic acidosis, likely correlated with shock or seizures (pH 7.114, pCO₂ 46.1 mmHg, HCO₃⁻ 14.8 mmol/L, Glu 65 mg/dL, Lac 12.4 mmol/L). A basic drug screen (SIGNIFY ER) was negative for all drugs. No increase in anion gap or osmotic pressure gap was observed.

Imaging examinations
Echocardiography in the ER demonstrated adequate cardiac contractility (ejection fraction) of 50% or above and an inferior vena cava diameter of 10/6 mm. On a body computed tomography (CT) scan about 2 h after taking the pills, a hyper-dense area in her stomach that was thought to be a drug clot was found. On a brain CT scan, there were no significant findings. An electrocardiogram showed sinus tachycardia, with a QRS of 119 ms and a QTc of 426 ms, without ischemic changes.

FINAL DIAGNOSIS
Acute drug intoxication with dextromethorphan.

TREATMENT
Upon arrival, the patient presented with symptoms of shock and altered consciousness; a significant infusion of extracellular fluid was swiftly initiated. The patient later developed recurrent generalized convulsions and status epilepticus, necessitating endotracheal intubation. We initiated the administration of noradrenaline as a vasopressor. Continuous administration of noradrenaline (maximum 0.2 µg/kg/min) increased blood pressure and halted the convulsions. A plain CT scan revealed a hyper-dense area in the patient’s stomach, thought to be a drug clot, approximately 2 h post-ingestion.
Subsequently, gastric lavage was performed, and activated charcoal was administered.

OUTCOME AND FOLLOW-UP

After admission to the intensive care unit and comprehensive management, we reduced the dose of vasopressors while confirming that mean arterial pressure was maintained at 65 mmHg or higher. On the 2nd hospital day, vasopressors were discontinued, and the patient was extubated because she was alert. Despite her overall stable condition, the patient was transferred to a psychiatric facility on the 3rd hospital day due to persistent suicidal ideation.

DISCUSSION

Dextromethorphan has long been utilized as an over-the-counter cough suppressant, available in various forms, including oral strips, lozenges, liquids and liquid-filled capsules, and in various formulations. The precise mechanism by which it suppresses coughing remains unclear. Despite structural similarities to opioid agonists, dextromethorphan does not exhibit significant activity at opioid receptors. Dextromethorphan acts on agonism at Sigma-1 receptors and is efficacious as an antitussive to an extent comparable to codeine but without the analgesic or habit-forming characteristics of codeine[14]. Dextromethorphan is a medication with a well-established safety profile when used in therapeutic doses[15].

In humans, dextromethorphan distribution volume is believed to be 5.0-6.7 L/kg[7]. Its protein binding rate is 65%[16]. The serum concentration of dextromethorphan peaks 2.5 h post-ingestion. The primary metabolite of dextromethorphan, dextrorphan, reaches peak plasma concentrations between 1.6-1.7 h after oral administration. The elimination half-life of the parent compound is approximately 2-4 h in individuals with typical metabolic function. Dextromethorphan and its metabolites are primarily excreted through renal elimination, with only very small amounts of fecal excretion[15].

Approximately 90% of individuals, classified as extensive metabolizers, experience rapid and extensive first-pass metabolism of dextromethorphan, resulting in the formation of the major O-demethylated metabolite dextrorphan, mediated by the enzyme CYP2D6. It is vital to note that the enzyme CYP2D6 is polymorphically expressed; some individuals lack activity (known as poor metabolizers), and others express enzyme activity at varying levels[15,17].

The dissociative properties of dextromethorphan are similar to those of ketamine and phencyclidine, owing to the cyclohexane ring and alkylated amine (features common in dissociative agents) found in its structure[15,19]. Dextromethorphan, in higher doses, has a mechanism of action similar to those of phencyclidine and ketamine, in that it antagonizes N-methyl-D-aspartic acid receptors by binding to the calcium ion channel. Blocking the N-methyl-D-aspartic acid receptors modulates excitatory neurotransmission, which brings about hallucinations, euphoria, dissociation, agitation, coma, “out-of-body” experiences and other neurobehavioral effects[1,7,20-22]. Additionally, dextromethorphan inhibits peripheral and central uptake of catecholamine, leading to adrenergic effects such as hypertension, tachycardia and diaphoresis[23]. The life-threatening toxicity associated with dextromethorphan abuse is caused by serotonin syndrome. Because of its serotonin reuptake inhibition properties, dextromethorphan can potentiate excessive body serotonin levels when used along with common prescription selective serotonin reuptake inhibitors or monoamine oxidase inhibitors, which can cause serotonin syndrome to develop[24-26].

Additionally, studies have identified various sites of action at which dextromethorphan and its metabolite dextrorphan interact, including antagonism at nicotinic receptors (α3b4, α4b2, a7), inhibiting serotonin and norepinephrine transporters and inhibiting voltage-gated calcium channels[24]. Other research has found that distinct symptoms occur within specific dosage ranges, which are known as plateaus[18]. Plateau 1 (100–250 mg) elicits a mild stimulant effect similar to that of methylenedioxyamphetamine. Plateau 2 (250-400 mg) is characterized by effects similar to concurrent ethanol and marijuana use, with some individuals experiencing hallucinations. Plateau 3 (450–800 mg) is associated with a dissociative “out-of-body” state akin to that produced by low recreational doses of ketamine. Plateau 4 (> 800 mg) produces a fully dissociative condition similar to ketamine intoxication. Dosages above 1800 mg have been associated with death. A unique study, based on comments left on YouTube videos, also lends credence to these findings[6].

The altered cognitive state brought about by dextromethorphan can lead to injuries. Therefore, a comprehensive assessment for indications of trauma should be a part of examinations[27]. Furthermore, the dissociative and hallucinogenic effects have been reported to potentially lead to suicide, assault and homicide among individuals who are addicted to the drug[28,29]. There are no definitive diagnostic tests for dextromethorphan poisoning, despite its widespread use and potential for abuse. As such, determining diagnoses may be difficult for patients with uncertain medical histories[30,31].

Shimozawa S et al. High doses of dextromethorphan inducing shock
For most patients, dextromethorphan toxicity can be effectively managed through supportive care, including monitoring of the airway, breathing and circulation, and hemodynamic monitoring. In some cases, airway protection may necessitate intubation with ventilator support, and sedation using medication and physical restraints may prove necessary in order to control agitation, violent behavior, and psychosis. When administered within an hour of ingestion, gastrointestinal decontamination with activated charcoal is the most effective treatment for dextromethorphan overdose. Naloxone may serve as a treatment for respiratory depression and central nervous system depression, but reports on its efficacy remain controversial. Due to the large volume of distribution and high protein binding rate of dextromethorphan, blood purification therapy is considered to be less effective for dextromethorphan toxicity.

In this instance, the convulsions were believed to have transpired as a result of a decline in cerebral perfusion pressure owing to shock. The possibility of distributive shock was considered, based on physical and echocardiographic findings. No elevation in blood pressure was detected, despite the administration of a significant volume of extracellular fluid. However, the infusion of noradrenaline raised the patient’s blood pressure and terminated the convulsive activity. Without appropriate treatment, the patient would have likely suffered cardiac arrest.

Although the possibility of symptoms arising from other drugs or additives cannot be ruled out, there have been no documented cases thus far (to the best of our knowledge) of shock resulting from dextromethorphan poisoning. Previous research has proposed that dextromethorphan functions as a voltage-gated calcium channel inhibitor among its potential sites of action. To date, no studies have shown sufficient evidence that these receptors are meaningfully activated by therapeutic doses. However, in this particular case, it is feasible that the high dose of 1665 mg, administered orally, augmented the calcium channel inhibitory effect. Blood purification was not deemed necessary, as the convulsions were swiftly mitigated through hemodynamic stabilization. However, it may prove efficacious in the event of severe symptoms.

Given that the patient in question was a petite woman, it is plausible that the dose of dextromethorphan in this scenario could have been lethal. Previous reports have attributed deaths to central nervous system depression and respiratory depression; however, shock may have been the causative factor in this particular instance. It is possible that we were merely fortuitous witnesses in the ER.

CONCLUSION

We reported the first case of shock caused by an overdose of dextromethorphan. Proper monitoring must be instituted when administering high doses of dextromethorphan, regardless of stable blood pressure, in anticipation of potential hemodynamic disturbances.

FOOTNOTES

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Conflict-of-interest statement: The authors declare that they have no conflict of interest.

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